

Medicinal **Chemistry**



Anti-anginal, Diuretics & anti-hypertensive agents

Anti-anginal

• These drugs are that prevent, terminate attacks of angina pectoris.-

• Angina pectoris -

• It is acute chest pain resulting from ↓ blood supply to the heart muscle.-

* Angina is caused by an accumulation of metabolites in the heart muscle.-

* Ischaemic heart disease is the most common serious health problem today.-

** Angina is a common symptoms for "Coronary (blood supply of heart muscle) heart disease" (CHD)-

Two principal forms of angina are recognized-

a. Classical angina (common form) → stable angina

- Attacks are predictable -

- induce by ⇒ Exercise, Emotion, Eating -

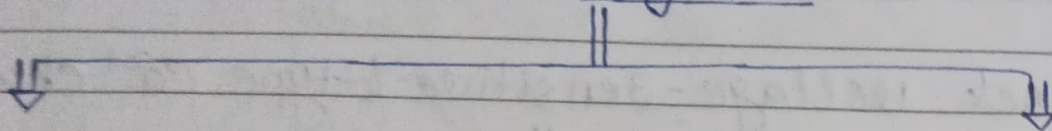
b. Variant/vasospastic angina - (uncommon form) -

→ unstable angina -

- Attacks are unpredictable -

- During sleep or rest -

16/08/2022

Classification of anti-anginal -

①. Vasodilators

eg- Nitroglycerin (GTN)*-

- Iso-sorbide dinitrate*-

- Amyl nitrite-

- Penta-erythritol-

- Dipyridamole-

②. Ca^{2+} channel blockers

eg- Verapamil, Diltiazem

- Diltiazem hydrochloride-

- Nifedipine, Amlodipine-

- Felodipine, Nicardipine

- Nimodipine-

Mechanisms of action (MOA) -①. Vaso-dilators - eg. Nitroglycerin (GTN) prototype

\Downarrow De-nitrated in the smooth
 \Downarrow muscle cell

• Release nitric oxide (NO) -



• Stimulate guanylyl cyclase -



• Increase cGMP -



• De-phosphorylation of myosin light chain -

• Decrease Ca^{2+} conc. in the cytosol -

• Relaxation of vascular smooth muscle fibres -

(B) Ca²⁺ channel blockers -

- Block voltage-sensitive L-type Ca²⁺ channel -



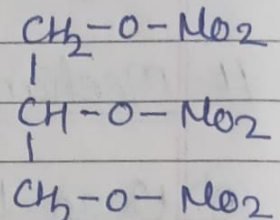
- Prevent entry of Ca²⁺ into the cell -



- Decrease contraction of smooth muscle -

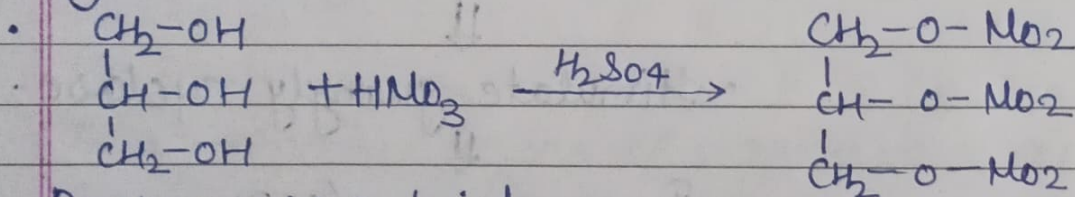
Synthesis of anti-anginal -

- Nitro-glycerine / Glycerol trinitrate *



1,2,3-propane triol tri-nitrate -

Synthesis -



Propane-1,2,3-triol

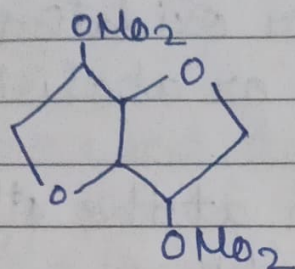
Nitroglycerine

Uses -

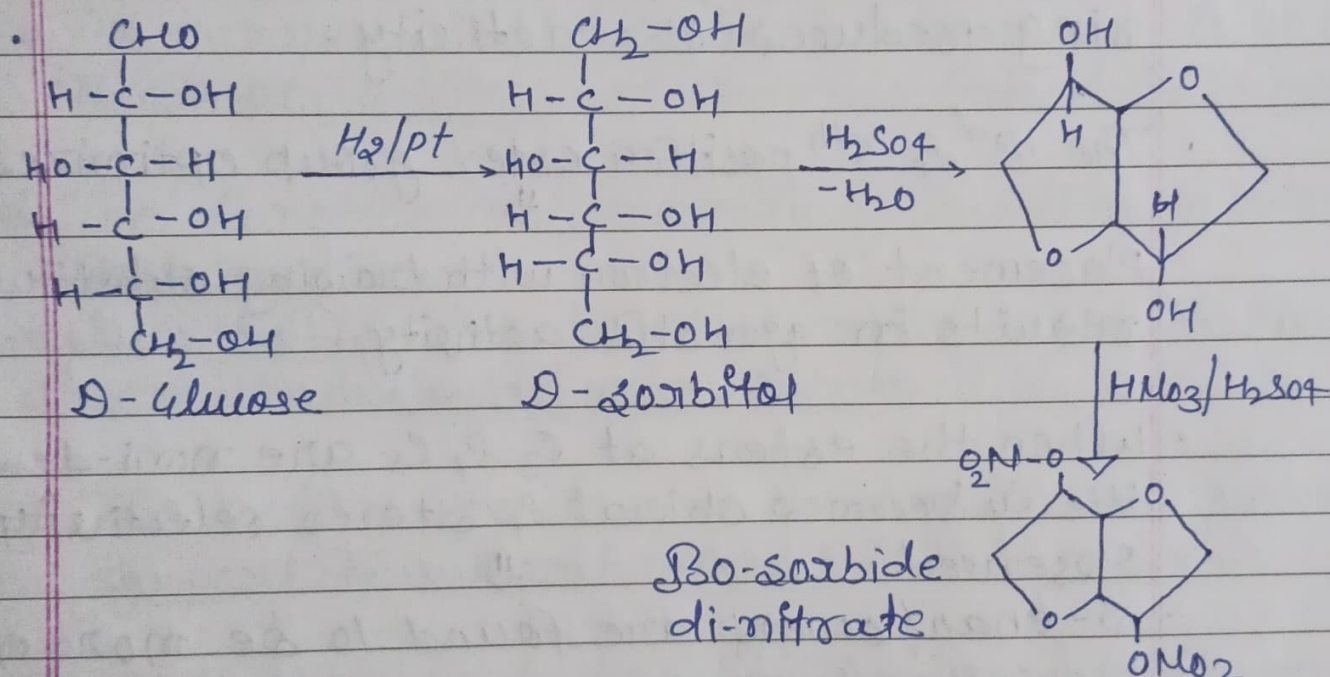
- It is used in angina pectoris & extensively as an explosive in dynamite. -
- It is used to prevent an explosion of the residue. -

16/08/2022

- Iso-sorbide dinitrate* (Isordil, Orbitrate) -



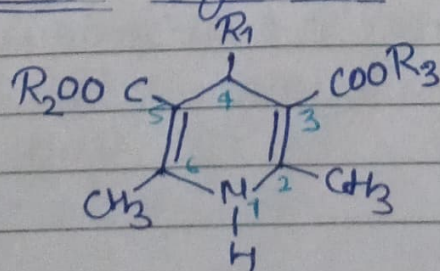
- Synthesis -



- Uses -

• It is effective in the treatment of acute angina attack. -

- # SAR of anti-anginal - (Dihydropyridines) -



1,4-Dihydro pyridines

- 1,4-dihydro pyridine ring is essential for activity.
- Substitution at N or oxidation or reduction of the ring reduces or abolishes the activity.
- A phenyl substitution at the 4th position is optimum for the activity.



Substitution at para or unsubstituted phenyl ring reduces the activity.

- The 3rd & 5th position ester group optimizes activity.



Placement of electron withdrawing substitution results in agonistic activity.

- When the esters at C₃ & C₅ are non-identical, the C₄ becomes chiral & stereo selectivity is observed.



- α -enantiomers are found to be more effective.